

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| APPLICANT: | UNGER |) | |
| SERIAL NO.: | 10/652,814 |) | EXAMINER: ILEANA POPA |
| FILED: | AUGUST 29, 2003 |) | ART UNIT: 1633 |
| TITLE: | NANOPARTICLE ENCAPSULATION SYSTEM AND METHODS |) | CONFIRMATION NO.: 2748 |

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Sir:

Applicant requests review of the final Office Action (mailed in the above-captioned application on November 13, 2008) for the reason(s) stated below. Claims 66, 67, 87-94, 101, and 133-141 were rejected under 35 U.S.C. § 102(c) as being anticipated by E. Unger et al. (U.S. Patent No. 6,139,819) as evidenced by Kondo et al. (Anal. Chem. 1991, 198:30-35, Abstract) and were rejected under § 103(a) over the same in combination with other references. Applicant submits that the Examiner's rejections contain clear deficiencies for both anticipation and obviousness, as explained below. All references herein to Applicant's prior Responses are incorporated herein by reference in their entireties.

1. The Examiner committed clear error in failing to consider Applicant-provided Federal Circuit case law, as well as MPEP guidance, for the rejection of claims 66, 67, 87-94, 101, and 133-141 under 35 U.S.C. § 102(c).

Applicant respectfully submits Examiner has committed clear error in the instant prosecution by misapplying and overlooking MPEP guidelines and overlooking precedential case law, as discussed below. It is submitted that the Examiner has taken the concept that patents are prior art for all they contain (MPEP § 2123) to erroneously conclude that a reference patent "clearly names the claimed species" if all of the claimed elements are disclosed. The Examiner appears unaware that there are further requirements for a *prima facie* case of anticipation beyond mere disclosure of elements, leading to clear error on the part of the Examiner. (Applicant reserves argument regarding disclosure of all the elements.)

It is submitted that the Examiner has improperly dismissed Applicant's arguments in the Responses dated 9/26/07 pages 17-21, and 6/11/08, pages 15-17. Applicant had argued that Federal Circuit and Board of Appeals decisions show that for a *prima facie* case of anticipation, the reference must disclose an embodiment with all the features of the claimed invention in their full detail and presented order. If the reference does not disclose an embodiment with all the features of the claimed invention in their full detail and presented order, then a second test is available, i.e., to assess whether the

totality of the reference provides a “pattern of preferences” which describes the claimed invention without the need for impermissible “picking and choosing.” See, e.g., *In re Arkley*, 455 F.2d 586 (CCPA 1972).

The Examiner has repudiated Applicant’s arguments by declaring that the MPEP contains no such teaching. On pages 16-17 of the Final Office Action dated 11/13/08, the Examiner states:

Applicant argues that, to be anticipatory, a reference (i) must disclose a specific embodiment which satisfies all the limitations of the claimed invention; this embodiment must be in the full detail and presented in the order of the claimed invention, and [sic—should be “or” per Applicant argument] (ii) the pattern of preferences disclosed in the reference must direct the ordinary artisan to the instant claimed invention. In response to this argument, it is noted that there is nothing in MPEP supporting such. . . Therefore, MPEP clearly states that (i) a reference which clearly names the claimed species anticipates the claimed invention no matter how many species are named, (ii) nonpreferred and alternative embodiments constitute prior art, and (iii) disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. [Examiner’s emphasis]

First, it is noted that the MPEP does have specific requirements for anticipatory disclosures:

“The identical invention must be shown in as complete detail as is contained in the ... claim.” *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). “The elements must be arranged as required by the claim....” *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990). MPEP § 2131.

Further, as argued in Applicant’s prior responses, the Patent Office must determine patentability in accordance with Federal Circuit law. The fundamental case *In re Arkley*, 455 F.2d 586 (CCPA 1972), requires that the cited reference “clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without any need for picking, choosing, and combining various disclosures.” *Id.* The Federal Circuit has applied *Arkley* repeatedly and widely, most recently, in *NetMoneyIn, Inc. v. Verisign, Inc.*, 545 F.3d 1359 (Fed. Cir. 2008):

“[U]nless a reference discloses within the four corners of the document not only all of the limitations claimed but also all of the limitations arranged or combined in the same way as recited in the claim, it cannot be said to prove prior invention of the thing claimed and, thus, cannot anticipate...[I]t is not enough that the [reference]...includes multiple, distinct teachings that the artisan might somehow combine to achieve the claimed invention....”(emphasis added) *Id.*

Multiple Board of Appeals and Interferences decisions also rely upon this and related case law, such as the (non-precedential) Board decision in *Ex parte Lettman* (discussed in the 6/11/08 Response at page 15) in which the Board, citing several Fed. Cir. cases, ruled that if a specific embodiment is not set out in the reference, the claimed invention will only be anticipated if the reference clearly and unequivocably directs the ordinary artisan to the claimed invention, without any need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference, and that such direction is provided within the “pattern of preferences” disclosed by the reference. The Examiner’s failure to consider and properly apply *In re Arkley* and its progeny, as well as

the teachings in the MPEP (see above quotation from MPEP § 2131), has resulted in clear error.

Applicant has extensively described the factual basis for failure of a *prima facie* case of anticipation. In the Response dated 6/11/08, pages 16-17, Applicant has described how Unger et al. does not teach a specific embodiment of the claimed reference that satisfies all the claim limitations of the instant claims. On pages 16-20, Applicant argues that the disclosures of E. Unger et al describe a large number of highly variable elements that can be combined in an almost limitless number of possible combinations, and further sets out, with extensive detail, the factual basis for why Unger et al does not direct the ordinary artisan to the claimed invention, such that the ordinary artisan would be able to "at once envisage" the claimed invention. These facts show that the totality of the teachings of Unger et al fails to provide a "pattern of preferences" which describes the claimed invention without the necessity for judicious selection from various disclosures thereof. E. Unger does not disclose an embodiment, even a non-preferred one, from which the ordinary artisan could "at once envisage" the claimed invention. It is therefore submitted that the Examiner has failed to properly consider Applicant's factual arguments. Reconsideration is respectfully requested.

2. The Examiner committed clear error in that Examiner has mis-read and mis-applied the *Atofina* case for the rejection of claims 66, 67, 87-94, 101, and 133-141 under 35 U.S.C. § 102(e).

In Responses dated 1/5/07, 9/26/07, and 6/11/08, Applicant had argued for the applicability of MPEP § 2131.03(II) relating to disclosure of ranges for anticipation, to the claims at issue. Specifically, the MPEP directs Examiners to be alert to the fact that where prior disclosure of a range merely "touches" or "overlaps" the prior art range, the prior art may **not** anticipate the claimed range, in view of case law:

Atofina v. Great Lakes Chem. Corp., 441 F.3d 991, 999, 78 USPQ2d 1417, 1423 (Fed. Cir. 2006) wherein the court held that a reference temperature range of 100-500 degrees C did not describe the claimed range of 330-450 degrees C with sufficient specificity to be anticipatory. Further, while there was a slight overlap between the reference's preferred range (150-350 degrees C) and the claimed range, that overlap was not sufficient for anticipation. MPEP § 2131.03(II)

The Examiner's response to Applicant's argument relating to *Atofina* is clear error because the Examiner mis-reads *Atofina*. Specifically, the Examiner states:

It is noted that in *Atofina*, the reference did not specifically recite a species with the claimed range, i.e., the reference did not positively recite a temperature of 330 or 450°C, nor did the reference positively recite a temperature within the claimed 330-450°C range. The instant case is different because the reference positively recites 30 nm, i.e., a species within the claimed range of "less than 50 nm"; such a recitation of a species within the claimed range was absent in *Atofina*. Because they positively disclose the species of 30 nm, which is less than 50 nm, Unger et al. anticipate the claimed range of "less than 50 nm." Final Office Action, page 23.

Examiner's assertion that "the reference [in *Atofina*] did not positively recite a temperature within the claimed 330-450°C range" is in fact flat-out wrong. In *Atofina*, the reference disclosed a preferred range of 150-350°C; the application claimed 330-450°C. MPEP 2131.01(II). There is a 20 degree range

(330-350°C) where the ranges overlap. Thus, contrary to the Examiner's assertion, in *Atofina* there is a positive recitation in the reference of a temperature (350°C) within the claimed range of 330-450°C. Accordingly, the Examiner's failure to consider the *Atofina* case was incorrect and failure to apply this case law to the instant claims is clear error. Reconsideration is respectfully requested.

Applicant has extensively described the factual basis for Applicant's arguments (i.e., that the instant facts are similar to the *Atofina* factual situation and *Atofina* applies in this situation, leading to the conclusion that there is no anticipation.) See, e.g., Responses dated 1/5/07, pages 14-16; 9/26/07, pages 21-23; 6/11/08, pages 23-24. Summarizing, the smallest liposomes disclosed in the working examples of E. Unger et al. are 200 nanometers (nm) diameter. The stated range of vesicles in the E. Unger disclosure is between 30 nm and about 100 micrometers (i.e., 100,000 nm). In contrast, Applicant's claimed particles have an average diameter of less than about 50 nm, a small fraction of overlap vis-a-vis E. Unger's generic range disclosure. Applicant's 50 nm or smaller particles are key to provide efficient caveolae uptake into cells (preventing destruction of the particles within the cells, see Example 2 of the instant specification.) In contrast, E. Unger et al. provides only generic (and not specific) support of his 30 nm threshold. Accordingly, the instant situation falls squarely within the scope of MPEP § 2131.03(II), necessitating that the Examiner undertake a determination as to anticipation specific to this particular case, which Examiner failed to do. This failure is clear error.

3. The Examiner's improperly dismisses Applicant's evidence by failing to provide evidentiary support for the rejection under 35 U.S.C. § 102(e).

Relevant particularly to Claims 94 and 138, the Examiner also contended that Unger et al "inherently" teaches a precipitate shell comprising a polypeptide and cationic precipitating agent, such as lithium. Applicant rebutted the Examiner's assertion as factually incorrect in the Response dated 6/11/08, pages 21-22. Specifically, Applicant extensively described how the E. Unger et al.-taught lithium aluminum hydride for coupling chemistry for reagent lipids (before their incorporation into the E. Unger liposomes) does not teach the inherent presence of Li⁺ ion, as E. Unger's Li⁺ ion is a side product that is removed in a quantitative extraction after the coupling reaction is complete. After Li⁺ is removed, only then is the reagent formed into liposomes. Thus, Applicant's factual argument showed that the final liposome will not inherently contain Li⁺. It is noted that MPEP § 2144.03(C) teaches:

Zurko, 258 F.3d at 1386, 59 USPQ2d at 1697 ("[T]he Board [or examiner] must point to some concrete evidence in the record in support of these findings" to satisfy the substantial evidence test). If the examiner is relying on personal knowledge to support the finding of what is known in the art, the examiner must provide an affidavit or declaration setting forth specific factual statements and explanation to support the finding. See 37 CFR 1.104(d)(2)).

However, it is noted that the Examiner did not provide concrete evidence or an affidavit or declaration in response to Applicant's evidence, instead merely repeating that because the E. Unger protein shell is exposed to aqueous Li⁺, "such exposure would necessarily result in precipitating the shell and the retention of the Li⁺ [in] the precipitated shell." Final Office Action, pages 19-20.

4. In view of the failure of the anticipation rejections, as explained above, there is clear error in the obviousness rejection

The Examiner committed clear error in the anticipation rejections. Therefore, the obviousness arguments also fail, as explained in detail in the Response dated 6/11/08, pages 25-33. The Examiner stated that the secondary references have nothing to remedy as the invention was anticipated by E. Unger et al., (Final Office Action, page 29). Accordingly, Examiner did not consider the Applicant's arguments against obviousness utilizing the secondary references, a clear error in view of the impropriety of the Examiner's anticipation rejections.

Finally, relating to the multiple non statutory double patenting rejections, it is noted that the rejections are based on both the instant application's parent patent application and Applicant's later-filed applications. It is submitted that Applicant will file a terminal disclaimer over the parent patent (although it is noted that as a continuation application, the instant application if granted a patent will expire on the same day as the parent), when all other rejections have been resolved. With respect to the nonstatutory double patenting rejections for Applicant's later filed copending applications, it is noted that MPEP §1490 (V)(D) dictates that "[i]f the provisional [nonstatutory double patenting] rejections in both applications are the only rejections remaining in those applications, the examiner should then withdraw the provisional [nonstatutory double patenting] rejection in the earlier-filed application thereby permitting that application to issue without need of a terminal disclaimer." It is submitted that as the instant claims exist in the "earlier-filed application," it is currently premature and improper to submit a terminal disclaimer over the later-filed copending applications.

In view of the above arguments, it is respectfully submitted that Claims 66, 67, 87-94, 101, and 133-141 are thus allowable and allowance of same is respectfully requested.

Dated: May 7, 2009

Respectfully submitted,

/Mary Breen Smith/

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| PRE-APPEAL BRIEF REQUEST FOR REVIEW | | Docket Number (Optional) 0269.01/C |
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| <p>Application Number 10/652,814</p> <p>First Named Inventor Gretchen M. Unger</p> <p>Art Unit 1633</p> | | <p>Filed August 29, 2003</p> <p>Examiner Ileana Popa</p> |

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).

Note: No more than five (5) pages may be provided.

I am the

- applicant/inventor.
- assignee of record of the entire interest.
See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.
(Form PTO/SB/96)
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/Mary Breen Smith/

Signature

Mary Breen Smith

Typed or printed name

303-268-0066

Telephone number

May 7, 2009

Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required.
Submit multiple forms if more than one signature is required, see below*.

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7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (*i.e.*, GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
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